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Q & A with Dr. Susan Swedo regarding PANDAS

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Dr. Susan Swedo, you could say, wrote the book on PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder). She is currently chief of the Pediatrics & Developmental Neuroscience Branch at the National Institute of Mental Health. In 1998, Swedo wrote the first paper on PANDAS. Click here for her official biography [1].

In the course of working on the story of the Le Roy illness, we contacted NIMH about her possible opinion on the Le Roy cases and discovered -- something that should have been obvious -- she can't publicly discuss the cases. With that in mind, *The Batavian* sent her eight questions we thought might be relevant to readers, but did not specifically address any patients in Le Roy. Below are the questions and Dr. Swedo's answers.

1. Has there ever been a case of mass PANDAS previous to this situation in Le Roy?

Not to my knowledge. It would be unlikely, given that PANDAS requires both a genetic susceptibility to post-streptococcal autoimmunity and a particularly virulent strain of strep. There have been epidemics of rheumatic fever and Sydenham chorea (the neurologic variant of rheumatic fever). Sydenham chorea is the model disorder for PANDAS, so it is theoretically possible that such an outbreak could occur.

2. Before Le Roy, would the suggestion of a mass outbreak be something you would have considered likely or even possible?

If a mass outbreak of PANDAS occurred, it should follow the same rules as individual cases, in which boys outnumber girls by 3-4 cases to 1. So if you had 14 affected girls, you would expect to have at least 40 to 50 boys exhibiting symptoms at the same time.

3. A neurologist from Mayo Clinic posted a video on YouTube that said about 1 percent of children develop tics. Dr. Mechtler said getting PANDAS is as much of a long shot as winning the lottery. And then imagine 12 diverse people all selecting the same numbers and winning the same lottery -- that's how unlikely it is the Le Roy situation is PANDAS. Others have reported that PANDAS isn't rare at all (there was an article in Scientific America). Which is it, rare or not?

PANDAS is not rare, but it is not common either. Obsessive-compulsive Disorder (OCD) affects about 1 in 100 students and PANDAS is not the most common cause of OCD (That cause is

currently unknown.). Among grade-school aged children, PANDAS may be responsible for a larger percentage of cases because the ratio of boys to girls is 3:1 before age 10, and then it switches at puberty so that becomes more common in girls than boys. Comorbid symptoms also differ by age with younger children frequently having a triad of OCD / ADHD (Attention-deficit Hyperactivity Disorder) and tic disorders, while adolescents and adults are more likely to have comorbid depression and/or anxiety disorders.

4. Is there anything about PANDAS that would make it more likely that mostly (all) girls would contract it?

See above. The opposite is true.

5. Is there evidence from previous cases of ties to environmental toxins? What environmental causes might be tied to PANDAS, if any?

No environmental causes have been suggested.

6. What is the most common way PANDAS is contracted?

PANDAS is the result of an untreated strep infection. The strep bacteria "hides" from the immune system by putting molecules on its cell wall that look like the human host (molecular mimicry). These foreign molecules are eventually recognized as part of the infecting strep infection and the child's immune system reacts to them, producing cross-reactive antibodies.

Cross-reactive antibodies are initially produced against a component of the strep bacteria but "misrecognize" a molecule in the child's own body as foreign and "attack it." In the case of rheumatic fever, the antibodies recognize molecules in the heart and cause rheumatic heart disease, or in the joints and cause arthritis, or in the brain (particularly the basal ganglia) and cause Sydenham chorea. Some children with cross-reactive "anti-brain" antibodies don't develop full-blown Sydenham chorea but develop PANDAS symptoms instead.

7. What about genetics might be related to a child getting PANDAS?

During the early 1900s, before antibiotic treatment was available for strep throat and scarlet fever, people would be quarantined for scarlet fever. Among the crowded tenements in NYC and Chicago, many people would get strep (scarlet fever or strep throat) but only one in 20 families would have a child who developed rheumatic fever. In those families, multiple children would often become affected with rheumatic fever and there are fascinating case reports of mothers with 10 of 11 children in the "Lying in" hospital (for rheumatic fever treatment) at the same time.

Those family histories are also present in PANDAS (increased susceptibility to rheumatic fever). In addition, the children have increased numbers of first-degree relatives with tics and/or OCD, suggesting that PANDAS may be due to a dual genetic vulnerability to post-streptococcal sequelae and OCD/tics.

8. The NIMH site says PANDAS can be contracted "to puberty," not "though puberty"? Is this a semantic difference or a significant difference? Is it known whether a child who has already reached puberty can contract PANDAS?

The PANDAS criteria were chosen to narrow the heterogeneity of OCD to a "studiable" cohort of patients. Puberty (or age 12 years) was chosen as the upper age limit because of immunologic evidence that about 98 percent of the population will have "immunity" to streptococcal infections

by the age of 12 years. We know that cases can occur after puberty, (because outbreaks of rheumatic fever and Sydenham chorea used to be common among military recruits and college students living in crowded dorms). Thus, PANDAS was defined as a pre-pubertal disorder but can occur through and after puberty.

(Dr. Swedo says) *Please note: PANS (*Pediatric Acute-onset Neuropsychiatric Syndrome*) criteria use a less restrictive term of "pediatric onset," which is variously defined as before age 18 years or age 21 years.*

Some additional information (below) that may be of interest: (I apologize that it's not already on the website. We're hoping to get it up by the end of the week.)

What is the best treatment for PANDAS?

The best treatment for PANDAS is to treat the inciting infection if it's still present (with antibiotics if strep is the cause). If there is no evidence for a current infection, some physicians have reported success with a short course of antibiotics (presumably because there is an occult infection in the sinuses, nasopharynx or elsewhere). In severe cases, a single course of plasmapheresis or intravenous immunoglobulin (IVIG) has been shown to be helpful. Although I've learned of physicians having success with use of steroids for PANDAS, we did not test them because of reports of worsening of tic disorders on steroids. (And in our studies of Sydenham chorea, the steroids produced only a temporary reduction in symptom severity with rebound to pre-treatment levels or worse after the steroids were stopped.)

How are tics diagnosed?

Tics are a very specific movement disorder in which there is a "premonitory urge" (feeling that you need to move, almost like an itch that makes you scratch it) and therefore, they can be at least partially controlled by the ticquer. Tics increase in times of stress and decrease during rest for most people (but sometimes the opposite occurs). They tend to wax and wane in severity over the course of an hour, day and weeks. Some children also have flurries of tics where they'll occur frequently and then not at all for a few minutes or even several hours. The most important aspect of a tic is its partially involuntary nature, where patients can exert some control over the symptoms (except for minor tics like eye-blinking and throat-clearing, which can occur more automatically). In general, if the tics are immediately noticeable to others, they should be at least partially controllable by the person who has them.

Also, tic disorders (like childhood-onset OCD) are about three times as common in boys as girls, so if you had a "Tic Epidemic," one would expect to see 40 to 60 boys if 14 girls were affected.

How is PANDAS/PANS diagnosed?

The updated clinical criteria for PANDAS are as follows:

1) Presence of obsessive-compulsive disorder and/or tic disorder;

2) Unusually abrupt onset of symptoms ("overnight," "0 to 60 in one to two days," "possessed by the illness");

3) Prepubertal onset (NOTE: This criterion was an arbitrary one chosen because post-streptococcal reactions are rare after age 12, but could occur in individuals who do not have protective immunity.);

4) Association with other neuropsychiatric symptoms, including various combinations of the following (NOTE: All would start suddenly and in combination in a previously healthy child):

a. Severe separation anxiety (can't leave parent's side, needs to sleep on floor next to their bed etc);

b. Generalized anxiety which may progress to episodes of panic and "terror-stricken look";

c. Motoric hyperactivity, abnormal movements and sense of restlessness;

d. Sensory abnormalities, including hypersensitivity to light or sounds, distortions of visual perceptions and, occasionally, visual or auditory hallucinations;

e. Concentration difficulties, loss of academic abilities, particularly in math and visuo-spatial skills;

f. Urinary frequency and new onset of bed-wetting;

g. Irritability (sometimes with aggression) and emotional lability. Abrupt onset of depression can also occur, with suicidal ideation;

h. Developmental regression, including temper tantrums, "baby talk" and handwriting deterioration (also related to motor symptoms).

5) Association with streptococcal infection. At initial onset, the symptoms may have followed an (asymptomatic and therefore untreated) streptococcal infection by several months or longer, so you might not find the inciting strep infection. However, on subsequent recurrences, the worsening of the neuropsychiatric symptoms may be the first sign of an occult strep infection (and prompt treatment may reduce the OCD and other symptoms).

FOR PANS – Criterion #1 is limited to OCD only (no tic disorders as primary diagnosis) and the last criterion is eliminated because PANS stands for Pediatric Acute-onset Neuropsychiatric Syndrome and does not include an etiologic component.

Le Roy [2]

Links:
[1] http://intramural.nimh.nih.gov/research/pi/pi_swedo_s.html
[2] http://thebatavian.com/leroy